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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/944,602	09/04/2001	Iris Pecker	01/22380	1723

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EXAMINER
DIBRINO, MARIANNE NMN

ART UNIT	PAPER NUMBER
1644	12

DATE MAILED: 08/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/944,602	Applicant(s) PECKER ET AL.	
	Examiner DiBrino Marianne	Art Unit 1644	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 7-10* is/are pending in the application.

4a) Of the above claim(s) *1,2 and 7-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Petition decision

DETAILED ACTION

1. Applicant's amendment filed 5/12/03 is acknowledged and has been entered.

Claim 3 is currently being examined.

The following is a new ground of rejection necessitated by Applicant's amendment filed 5/12/03.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not disclose how to practice the method of diagnosing CLL or NHL in a human individual suspected of suffering from a blood cancer, comprising monitoring an expression of heparanase in white blood cells of the individual, wherein the absence of said expression of heparanase indicates a positive CLL or NHL diagnosis. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass methods of diagnosing CLL or NHL in a human comprising monitoring any heparanase expression besides one that is not SEQ ID NO: 1 and wherein the lack of expression of said heparanase is not specifically indicative of the recited conditions.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to the instant rejection are the scope of the claim, unpredictability in the art, the amount of experimentation required, and the amount of direction or guidance presented.

The instant specification discloses that PWBC (peripheral white blood cells) from patients with CML, ALL, or AML were tested for the expression of the human hpa gene by rtPCR of total RNA using cDNA primers from SEQ ID NO: 1 of the instant application, i.e., using SEQ ID NO: 6 and SEQ ID NO: 7, with the result that 31/31 CLL patients and 4/4 NHL patients PWBC tested negative, whereas 14/14 AML and 2/2 ALL patients PWBC tested positive, and 1/3 CML patients PWBC tested positive and 2/3 tested negative (figure 13 and page 56-57 and Table 1 on page 58). However, it is clear that the claimed method alone is insufficient to determine whether a patient has CLL or NHL. 2/3 CML patients PWBC had

absence of heparanase expression, the number of patients PWBC tested is very small, and conditions that are heterogeneous and/or are in different stages of progression are being assessed with the claimed method. Evidentiary reference The Merck Manual (16th Edition) teaches that NHL is a heterogeneous group of diseases consisting of neoplastic proliferation of lymphoid cells that usually disseminate through out the body (especially page 1248). Evidentiary reference The Merck Manual (16th Edition) teaches that CLL is most commonly a B cell form, but that it can also occur in a T cell form and that other chronic leukemic patterns have been categorized under CLL, i.e., it is a heterogeneous group of diseases with different stages (especially page 1242). Evidentiary reference The Merck Manual (16th Edition) does not teach diagnosis of CLL or NHL comprising monitoring expression of heparanase in WBC. Both CLL and NHL are disclosed to be negative for heparanase expression, therefore one of skill in the art could not distinguish whether a patient had CLL or NHL solely on the basis of the test that indicates that the hpa gene product is not expressed in PWBC. Therefore, it is clear that additional factors must be considered in determining whether a patient has one of these diseases, and said factors are known to one of skill in the art as indicated by the methods of diagnosing the conditions as evidenced by The Merck Manual.

In addition, the specification further discloses that previous measurements of heparanase activity, i.e., expression and secretion, as measured by conversion of high MW HSPG substrate (pages 7, 8 and 56), indicate that AML and CML, but not CLL PWBC are positive. The specification discloses that use of RT-PCR with the heparanase specific primers from SEQ ID NO: 1 enables a more sensitive and rapid determination of hpa gene expression by human leukemia and lymphoma cells. However, 2/3 CML patients PWBC were negative using RT-PCR (Table 1), a more sensitive test than activity measurement as defined supra which is disclosed to have yielded positive results in all CML patients, indicating a lack of concordance. The specification does not disclose activity level in NHL.

The instant specification discloses that potential existence of other human heparanases distinct from the human heparanase encoded by SEQ ID NO: 1, but that one other human heparanase is expressed in human placenta (especially pages 10-11).

There is insufficient guidance in the specification as to how to practice the method of the instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

Applicant's comments in the amendment filed 5/12/03 have been fully considered but are not persuasive. Applicant's arguments are of record in the said amendment, and the Examiner has addressed them in the instant rejection.

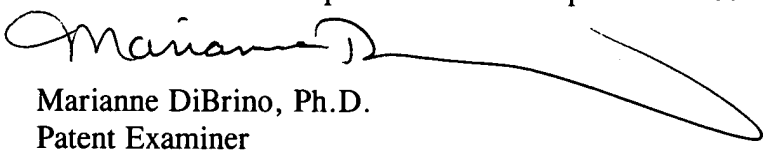
4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

5. Applicant states on page 3 of Applicant's amendment filed 5/12/03 that an IDS is being submitted under separate cover. Said IDS has not been received at the present time.

6. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 703-308-0061. The Examiner can normally be reached on Monday and Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



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July 31, 2003

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